

## REMARKS

### Summary of the Invention

The invention features methods for identifying the activity range of modulators of the biological activity of a CeSERT and for identifying test compounds that modulate the activity of secondary targets that alter the uptake of serotonin by a SERT.

### Support for the Amendments

Support for new claim 12 is found on page 34, line 25, through page 35, line 10, and page 37, lines 20-24, of the specification.

### Summary of the Office Action

Claims 1-11 are pending and stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement.

### Declaration

The Examiner states that the Declaration filed in this case does not provide the signature for one of the inventors. In reply, Applicants submit herewith a copy of the Declaration that was submitted to the Patent Office on July 31, 2001. This document includes the signatures of both inventors, which are present on two separate copies of page 2 of the Declaration.

### Drawings

Applicants note the objection to the drawings and will submit corrected drawings upon

notice of allowable subject matter.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-11 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner states that:

The working examples include one single mutant mod-5 CeSERT (n3314)...[while] claim 6 is drawn to three mutants mod-5 CeSERT (n3314), mod-5 CeSERT (n822), and mod-5 CeSERT (n823). There is no indication in the specification that could provide evidence to the artisan that [the] two other mutants are also used to test the activity range of a compound...[and] the specification does not teach about the behavior of [the] two other mutants in relation to a test compound.

Applicants respectfully traverse this rejection.

Applicants are puzzled by the Examiner's statement that "[t]here is no indication in the specification that could provide evidence to the artisan that [the] two other mutants are also used to test the activity range of a compound." The specification clearly states on page 41, lines 28-30, that "[a] nematode expressing either a wild-type or mutant *C. elegans* CeSERT gene, such as CeSERT (n823), CeSERT (n822), or CeSERT (n3314), is exposed to a test compound." Therefore, one of ordinary skill in the art would have recognized, based on the specification at the time the invention was made, that the other mutant CeSERT-containing nematodes could also be used to test the activity range of a compound.

Applicants point out that:

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with the information known in the art without undue experimentation. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.* 802 F.2d. 1318 (Fed. Cir. 1985).

Applicants submit that the invention satisfies this test for enablement. The specification, on pages 41-42, clearly describes the steps of exposing a first nematode (e.g., a mutant CeSERT containing nematode) and a second nematode (e.g., a wild-type CeSERT containing nematode) to a test compound and observing the behavior of the first and second nematodes. The specification, on page 42, lines 14-17, describes the various behaviors that can be monitored as swimming, locomotion, pharyngeal pumping, egg-laying, nose contraction, and defecation. A comparison of the observed behavior of the first and second nematode allows one to determine the activity range of the compound being tested. Performing these steps in the instant method would require nothing more than routine experimentation.

The Examiner, however, states that “the specification does not teach about the behavior of [the] two other mutants in relation to a test compound.” The M.P.E.P. § 2164.02 states that:

Compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed...The specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970).

Applicants submit that the specification clearly describes various relevant nematode behaviors, discussed above, that can be observed and used to determine the activity range of a test compound, as recited in the method of instant claim 1. Applicants argue that all that is necessary to practice the instant method is the ability to determine the presence, absence, or relative degree of these behaviors. Furthermore, contrary to the Examiner’s statement above, the specification does describe on page 21, line 1, through page 23, line 3, two behaviors, locomotion and

swimming, of the CeSERT (*n822*) and CeSERT (*n823*) mutants. Using this description and the information provided in the specification, one skilled in the art could reasonably observe and identify these and other behaviors of mutant CeSERT-containing nematodes in the presence of a test compound, and would certainly not require prior knowledge of the effect of the test compound on the mutant nematode to practice the instant invention, as suggested by the Examiner.

The Examiner also states that:

the specification does not provide any evidence of testing the compound for a mutant animal in the presence of [a] second animal and studying the defined behavior of [the] first animal against [the] second animal. A test compound at a particular concentration will have [a] different effect on [the] first nematode behavior when tested in the presence of [the] second nematode because [the] second nematode may interfere...[with] the effect of a particular concentration of a test compound against [the] first nematode.

Applicants respectfully traverse this rejection.

The instant methods do not recite contacting a first nematode with a test compound in the presence of a second nematode, as suggested by the Examiner. Applicants have amended claim 1 to recite “comparing said defined behavior of said first nematode to the defined behavior of a second nematode not contacted with said compound” to clarify this feature of the instant method. Applicants direct the Examiner to page 41, line 25, through page 42, line 17, of the specification, which describes the assay method recited in the instant claims. Using this method, 20 nematodes are placed into a single well of a 96-well polystyrene plate containing a test compound, and a behavior, or the lack thereof, is determined. The specification explains on page 42, lines 6-7, that the number of nematodes exhibiting a behavior in a well containing the test compound is

then compared to the number of nematodes exhibiting that behavior in a well that lacks the compound. Based on the description in the specification, the first nematode is not tested in the presence of the second nematode. Therefore, the second nematode cannot interfere with the effect of the test compound on the first nematode, as suggested by the Examiner.

Based on the foregoing statements, Applicants respectfully request the withdrawal of the rejection of claims 1-11 under 35 U.S.C. § 112, first paragraph.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. Applicants note that the Examiner's Action was mailed to the incorrect address. Effective immediately, please address all communication in this application to:

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Enclosed is a petition to extend the period for replying for two months, to and including June 3, 2002, as June 2, 2002 falls on a Sunday.

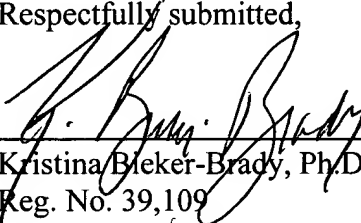
If there are any charges or any credits, please apply them to Deposit Account No. 03-

2095

Date:

May 29, 2002

Respectfully submitted,

  
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Version with markings to show changes made

1. (Amended) A method for determining the activity range of a test compound, which modulates the uptake of serotonin by a serotonin reuptake transporter (SERT), against a secondary target, said method comprising the steps of:

(a) contacting a first nematode expressing a mutated *Caenorhabditis elegans* SERT (CeSERT) polypeptide, wherein said mutated CeSERT polypeptide has a reduced capacity to take up serotonin relative to wild-type, with said compound;

(b) assaying a defined behavior of said first nematode; and

(c) [assaying said defined behavior of a second nematode not contacted with said compound; and

(d)] comparing said defined behavior of said first nematode to the defined behavior of a [said] second nematode not contacted with said compound, wherein a difference in said defined behavior between said first and second nematode indicates that said compound has a secondary target.

2. (Amended) The method of either claim 1 or 12, wherein steps (a) to (c) [(d)] are repeated using first and second nematodes selected from a panel of nematodes expressing mutant CeSERT polypeptides, wherein said mutant CeSERT polypeptides differ from said mutated CeSERT polypeptide of step (a).

3. (Amended) The method of either claim 1 or 12, wherein said mutated CeSERT polypeptide is a complete loss-of-function.

4. (Amended) The method of either claim 1 or 12, wherein said method comprises a liquid locomotion assay.

5. (Amended) The method of either claim 1 or 12, wherein said defined behavior is movement, pharyngeal pumping, egg-laying, nose contraction, or defecation.

6. (Amended) The method of either claim 1 or 12, wherein said mutated CeSERT polypeptide is selected from the group consisting of a CeSERT(*n822*) polypeptide, a CeSERT(*n823*) polypeptide, and a CeSERT(*n3314*) polypeptide.

7. (Amended) The method of either claim 1 or 12, wherein said compound is from a class of compounds selected from a group consisting of antidepressants, migraine medications, and anti-emetics.

11. (Amended) The method of either claim 1 or 12, wherein said test compound is administered at more than one concentration.